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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/260,624	03/01/99	OHNISHI T	A-67648-1/RF

HM12/0801
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EXAMINER	
SCHMIDT,M	
ART UNIT	**PAPER NUMBER**
1635	11

DATE MAILED: 08/01/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
02/269,624	Ohnishi
Examiner	**Group Art Unit**
Schmidt	1635

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 5/12/00.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-6, 8-28 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 1-6, 8-28 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of References Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other_____

Office Action Summary

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-6 and 8-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for localized delivery of Rad51 to a mouse and treatment effects, does not reasonably provide enablement for any method of administration and treatment of any whole organism as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and practice the invention commensurate in scope with these claims for the same reasons of record as set forth in the Official action mailed 11/08/99.

Applicant's arguments filed 5/12/00 have been fully considered but they are not persuasive. New claims 15-28 were added which specify administration of the antisense to local sites in the whole organism, such as to a tumor, and via injection. However, the claims still read on delivery of Rad51 antisense to any whole organism. The specification suggests on page 8 that the patient is usually a human, but may also be rodents, cats, dogs, rabbits, farm animals or primates.

Applicant points out on page 5 of the response filed 5/12/00 that "the test of enablement is whether one of ordinary skill in the art would be able to make and use the claimed invention

without undue experimentation, based on the disclosure and the prevailing knowledge in the field." Applicant then submits on page 6 that "the primary obstacles that the use of antisense nucleic acids face are essentially the same as all nucleotides used for gene therapy. The ever-accumulating knowledge in the field, along with the teachings provided in the present application, provide substantial guidance for the skilled artisan to practice the present claims." Applicant later cites the Wands factors on page 11 to show the factors for consideration for a *prima facie* case of lack of enablement.

Applicant argues on page 12 that "practicing the present methods is not "undue experimentation" since the Board affirmed that it was not undue experimentation to make monoclonal antibodies via the steps recited on page 13 of the response. The steps taught in the creation of monoclonal antibodies, however, are not analogous to the steps one skilled in the art would take to practice the instant invention. Further, several of the factors considered unpredictable in the art were argued in the previous Official action to show that one skilled in the art would not find the necessary guidance in the specification or the art to discern the necessary steps for administration of antisense oligonucleotides to any whole organism for the claimed therapeutic functions.

Applicant argues that Flanagan and others in the art teach liposomal administration of gene therapeutic agents to whole organisms, that all drugs show some degradation, that Flanagan teaches delivery of oligonucleotides to specific regions in whole organisms, and that "the skilled artisan knows that introduction of the nucleotides in close proximity to a target increases the

amount of nucleotide that will actually reach the target." The examples cited however do not serve to provide one skilled in the art with guidance as to how to generally formulate and administer any Rad51 antisense oligonucleotide to any whole organism as broadly claimed for therapeutic functions. Yes there are limited successes of nucleic acid administration to whole organisms for therapeutic purposes, but the protocols are not so general as to apply broadly to any nucleic acid administration to any whole organism. Note McCluskie et al. who teach in the analogous art of DNA vaccines that administration of the same nucleic acid vaccines to different, but related whole organisms had widely varying effects. The previous Official action cited Branch and Flanagan in particular because they teach the difficulty involved in the administration of antisense oligonucleotides. Antisense oligonucleotides when administered to whole organisms have specific issues with non-selective binding leading to toxicity for instance. As argued previously, the art is not clear at the present time as to how one skilled in the art would make and administer specific nucleic acids such as antisense to whole organisms for the scope of treatments instantly claimed.

Applicant does point out that in present examples, "the nucleotides are injected into the cisterna magna where the tumor resides." Both the specification and Taki et al. (previously cited under a 35 USC 102 rejection) teach that such injection, in combination with other cancer treatments functioned as a therapy for certain tumors in mice. However, as argued in the previous Official action, such guidance would still lead one of skill in the art to practice undue experimentation to make and use such antisense in other whole organisms. Specifically, Crystal

was cited to teach that results in mice do not necessarily correlate to results in humans. Mc Cluskie et al. are further cited as further support.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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